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Claim 17

TITLE: Family of mammalian potassium channels, their cloning and their use,
especially for the screening of drugs

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INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Duprat, Fabrice	Vallauris		FR	
Lesage, Florian	Paris		FR	
Fink, Michel	La Bocca		FR	
Lazdunski, Michel	Nice		FR	

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CLAIMS:

1. An isolated and purified nucleic acid molecule coding for a protein having a potassium (K.sup.+) permeable membrane, comprising more than one P domains and three, four, five or more than six transmembrane segments.
2. The nucleic acid molecule of claim 1 coding for a protein wherein the number of P domains is two and the number of transmembrane segments is four.
3. The nucleic acid molecule of claim 1 which is human.
4. The nucleic acid molecule of claim 1 which is a cDNA copy of a 2.6 kilobase transcript expressed at high levels in the pancreas and placenta, and at lower levels in the brain, lung, prostate, heart, kidney, uterus small intestine and colon.
5. The nucleic acid sequence of claim 1 which codes for a protein which comprises the sequence represented by SEQ ID No. 4.
6. The isolated and purified nucleic acid sequence of claim 1 which codes for a protein which comprises the s equence represented by SEQ ID No. 4 or the functionally equivalent sequence thereof which comprises two P domains and four transmembrane segments.
7. An isolated and purified nucleic acid sequence of claim 2 which comprises our open reading frame (ORF) of 1185 nucleotides.
8. The isolated and purified nucleic acid sequence of claim 7 which is human.
9. An isolated and purified protein having a potassium (K.sup.+) permeable membrane comprising more than one P domain and three, four, five or more than six transmembrane segments.
10. The protein of claim 9 wherein the number of P domains is two and the number of

transmembrane segments is four.

11. The protein of claim 10 in which the potassium transport channel exhibits outward rectification when the extracellular concentration of potassium is 2 mM and no rectification when the extracellular potassium is 98 mM, thereby evidencing lack of intrinsic voltage sensitivity

12. The protein of claim 10 in which the potassium transport channel lacks intrinsic voltage, lacks kinetics voltage- and time sensitivities, thereby evidencing characteristics of background conductance.

13. The protein of claim 9 in which the activity of the potassium transport channel is regulated by extracellular pH in a physiological range of 6.5 and 7.8.

14. The protein of claim 13 which the potassium channel exhibits 10% transport activity at pH 6.7, and 90% transport activity at pH 7.7.

15. The protein of claim 14 which is human.

16. The protein of claim 15 which comprises the sequence represented by SEQ ID No. 4.

17. A method of screening for substances capable of modulating the activity of the potassium transport channel encoded by the nucleic acid sequence of claim 1 comprising contacting pre-selected amounts of the substance to be tested with cells expressing the potassium transport channel, measuring the effects of said substance on the transport functions of the potassium transport channel, and identifying the substance that has a positive or negative effect on potassium channel activity.

18. A substance, identified by the method of claim 17 that is competent to positively or negatively influence the transport functions of a potassium transport channel.

19. A method for identifying genetic polymorphisms in the locus comprising the nucleic acid sequence of claim 1 by hybridizing DNA samples under stringent conditions with a probe comprising the isolated nucleic acid sequence encoding the potassium transport channel.

20. The method of claim 19 where the probe is hybridized to intact chromosomes in situ.

21. The method of claim 20 where the probe is hybridized with Southern blots of genomic DNA digested with a restriction endonuclease.

22. The method of claim 17 wherein the nucleic acid sequence encodes a protein in which the potassium transport channel lacks kinetics, voltage- and time-sensitivities, thereby evidencing characteristics of background conductance.

23. A substance identified by the method of claim 22 which is competent to positively or negatively influence the transport functions of a potassium transport channel.

24. A self replicating vector comprising the nucleic acid molecule of claim 1.

25. A cell transformed with the vector of claim 24, which cell is selected from the group consisting of prokaryotes and eukaryotes.

26. The transformed cell of claim 25 which is a yeast, insect cell, plant cell or mammalian cell.

27. The transformed cell of claim 25 which is a bacteria.

28. A method for the expression and isolation of a potassium transport channel encoded by the nucleic acid molecule of claim 1 in a competent host cell comprising transferring the vector of claim 24 into a competent host cell, culturing said host

cell under conditions allowing the production of the potassium transport channel, and isolating and purifying the polypeptide comprising the potassium transport channel.

29. A transgenic animal which comprises the nucleic acid sequence of claim 1 encoding a potassium transport channel.

30. The transgenic animal of claim 29 in which the nucleic acid sequence encoding the potassium transport channel is non-human.

31. The transgenic animal of claim 29 which overexpresses the potassium transport channel encoded by the nucleic acid sequence represented by SEQ ID No. 3.

32. The transgenic animal of claim 29 which is deficient in the expression of the potassium transport channel encoded by the nucleic acid sequence represented by SEQ ID No. 3.

33. A pharmaceutical composition for the treatment of diseases caused by a defective potassium transport or a deficiency of the potassium transport protein comprising the nucleic acid of claim 1 or the transformed cells of claim 25 in one or more tissues having a defective potassium transport function under conditions which allow for the expression of the potassium transport channel in said tissue.